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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,343	06/19/2001	Michael E. Stiles	C60007.1US	1463

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EXAMINER	
KINSEY, NICOLE	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/883,343	STILES ET AL.	
	Examiner	Art Unit	
	Nicole E. Kinsey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,20 and 37-54* is/are pending in the application.

4a) Of the above claim(s) *18,20 and 41-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-40 and 50-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Nicole Kinsey, PhD, Group Art Unit 1648.

Withdrawn Rejections

The rejection of claim 39 under 35 USC 112, second paragraph, has been withdrawn in view of applicants' amendment to claim 39 to delete the term "heterologous."

The rejection of claims 37-39 under 35 USC 102(a) as being anticipated by McCormick et al. has been withdrawn in view of applicants arguments. In particular, McCormick et al. was published after applicants' effective filing date, and is thus, not prior art. This also applies, in part, to the rejection of claim 40 under 35 USC 103(a) as being unpatentable over McCormick et al.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-40 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection directed at the genus of "operable muteins" recited in the claims.

The specification fully describes the structure of the signal peptide of divergicin A. However, the specification does not teach the structure of any "operable muteins thereof," nor teach what parts of the structure are important for operability. Considering the unpredictable effects of any sequence change upon the function of this polypeptide, and the lack of any art-recognized correlation between the amino acid sequence and the functional activity of this polypeptide, it is concluded that the specification does not reasonably convey that applicants possessed the "operable muteins" recited in the claims.

Applicants argue that one skilled in the art would readily recognize what is meant by "an operable mutein thereof."

Applicants' argument has been fully considered, but is not found persuasive. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function

correlation, methods of making the claimed product, or any combination thereof. In this case, the only factors present are the function and structure of the signal peptide of divergicin A. With regard to any mutein, the only factor present in the specification is the function of the mutein (i.e., bacteriocinogenic activity). The specification does not teach the structure of any "operable mutein thereof" included in the genus, nor identifies any particular portion of the structure that must be conserved for operability. In addition, the specification does not provide sufficient guidance for making a mutein (i.e., which amino acids can vary and still maintain the required function?). Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of muteins, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making it. The

compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to a lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the divergincin A sequence set forth in the specification meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-40 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claim 38 is indefinite because of the recitation "an operable mutein thereof." The specification does not indicate what characteristics distinguish an operable mutein of the divergicin A processing peptide from any operable signal peptide or leader peptide. Therefore, the metes and bounds of the claimed subject matter are unclear, and the claim is indefinite.

Applicants argue that "mutein" is defined at page 14, line 25+ as a "conservative variation" and provides as an example a difference of "1-4 amino acid residues." Most importantly, the muteins "must exhibit bacteriocinogenic activity (page 15, line 1), regardless of the number of differences between the mutein and the native divergicin A processing peptide. Applicants further argue that creating and determining a particular mutein of divergicin A is routine and simple.

Applicants' arguments have been fully considered, but are not found persuasive. Because the specification does not teach the structure of any "operable mutein thereof," nor identifies any particular portion of the structure that can be mutated or that must be conserved for operability, one cannot determine the structure of a mutein. The specification does not indicate what characteristics distinguish an operable mutein of the divergicin A processing peptide from any operable signal peptide or leader peptide. Therefore, the metes and bounds of the claimed subject matter are unclear, and the claims are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37-39 remain rejected under 35 U.S.C. 102(b) as being anticipated by Worobo et al (Journal of Bacteriology 177:3143-3149, 6/95). This rejection applies to new claims 50, 52 and 54.

The reference teaches inhibiting the growth of susceptible bacteria in an environment, using cells transformed with an expression vector encoding divergicin A signal peptide, divergicin A bacteriocin, and divergicin immunity, see for example pRW5.6 transformants in Figure 3. The reference therefore meets each and every limitation of the claims.

Applicants argue that Worobo et al. does not teach a construct containing a promoter, a divergcin, and a signal peptide (Applicants acknowledge that Worobo et al. teaches a construct containing a promoter and a divergicin). Applicants' argument is not found persuasive.

Contrary to applicants' assertion, Worobo et al. teaches pRW5.6 which contains a promoter from pGKV259 and the 514-bp EcoRV-AccI fragment of pCD3.4. Figure 1 depicts the 514-bp fragment, which contains a divergicin gene and an N-terminal extension prior to the divergicin gene. Worobo et al. characterized this N-terminal extension as a signal peptide (see page 3147, especially right column and Figure 4). Worobo et al. states that "[t]he 29-amino acid N-terminal region of divergicin complies with all of the Von Heijne rules for a signal peptide." Worobo et al. further states that "[c]onclusive evidence that the N-terminal extension of divergicin acts as a signal peptide was achieved with the production of alkaline phosphatase in *E. coli* when the

native signal peptide was replaced by that of divergicin" (see page 3148, first full paragraph). Therefore, pRW5.6 contains all elements recited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 40 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Worobo et al (Journal of Bacteriology 177:3143-3149, 6/95).

The claim is drawn to a vector encoding a plurality of different bacteriocins.

On page 3143 of Worobo et al, the reference discusses production of two or more bacteriocins within gene cassettes, and on page 3148 suggests fusions of the divergicin signal peptide with other bacteriocins for secretion without specific secretion and maturation proteins.

It would have been obvious for one of ordinary skill in the art to carry out the suggestions made in the reference, i.e., to fuse the divergicin signal peptide to the structural gene of another bacteriocin in a gene cassette, and to combine two gene cassettes to produce two or more bacteriocins from a single vector. There would have been a reasonable expectation of success given the fact that fusion proteins and expression cassettes are routinely made in the art. Thus, the invention as a whole is *prima facie* obvious, absent unexpected results.

Applicants argue that Worobo et al. does not teach the expression of a single bacteriocin under the control of a bacteriocin processing peptide. Applicants' arguments have been addressed above (see rejection under 35 U.S.C. 102(b)).

Claims 51 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Worobo et al (Journal of Bacteriology 177:3143-3149, 6/95).

The claims are drawn to a construct containing a bacteriocin selected from leucocin, enterocin, and colicin V and containing a p32 promoter.

The teachings of Worobo et al. are outlined above. Worobo et al. does not teach the various bacteriocins or the p32 promoter. However, it would have been obvious for one of ordinary skill in the art to substitute any known bacteriocin in place of divergicin

in the construct of Worobo et al. and based on the teachings of Worobo et al., the results would have been predictable. Further, it would have been obvious for one of ordinary skill in the art to substitute one promoter for another. The choice of promoter (e.g., prokaryotic, eukaryotic, inducible, etc.) is well within the purview of the ordinary skilled artisan. Therefore, it would have been obvious to select a different prokaryotic promoter such as the p32 promoter of lactococcus to use in the construct of Worobo et al. Thus, the invention as a whole is *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37-40 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,403,082. The rejection also applies to new claims 50-54.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the application claims (1) encompass the subject matter of the patented claims and/or (2) are drawn to embodiments of the patented subject matter which are obvious embodiments when the patent claims are viewed in light of the supporting disclosure.

Applicants argue that the claims of the instant application are much broader than the claims of the cited patent.

Not only are the instant claims broader in scope, but the instant claims (genus) also encompass the scope of the patented claims (species). For example, if one of ordinary skill in the art practices the method of patented claim 1, the construct created would also read on the construct of instant claim 37. Further, selecting brochocin-C as the bacteriocin is an obvious substitution with predictable results (see 35 U.S.C. 103(a) rejection above regarding choosing a bacteriocin).

The species claimed in the patented claims anticipate the instantly claimed genus, and therefore, a patent to the genus would, necessarily, extend the rights of the patented species claims.

No claim is allowed.

Conclusion

Applicants' amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole E. Kinsey, Ph.D. whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nicole E. Kinsey, Ph.D.
Examiner
Art Unit 1648

/nk/

/Stacy B. Chen/ 8-17-2007
Primary Examiner, TC1600